REPORT TO CONGRESS

Health-Related Research and Development Activities at USAID

An Update on the Five-Year Strategy, 2006–2010

HIV/AIDS – MICROBICIDES DEVELOPMENT

October | 2010

HIV/AIDS

Issues and Rationale

Worldwide, an estimated 33 million people are living with HIV; 22 million of these individuals live in sub-Saharan Africa alone. Women are at increased risk, making up more than half of all global cases of HIV/AIDS, and 60 percent of the cases in sub-Saharan Africa.

Despite their great risk, many women in developing countries have difficulty protecting themselves from HIV infection through conventional prevention methods such as negotiating delay of sexual debut, partner reduction, and condom use, indicating that no single approach to HIV/AIDS prevention is likely to have a dramatic impact. Integrated approaches to prevention, detection, and management that are tailored to a specific country context and populations at risk yield the best results. Novel tools to prevent new HIV infections could complement currently available methods.

Areas of Research and Introduction

USAID supports innovative biomedical research to develop and introduce new products and technologies, such as vaccines and microbicides, to prevent HIV transmission, thereby mitigating the burden of HIV/AIDS in developing countries. USAID also supports applied and operations research while conducting public health evaluations to improve HIV/AIDS intervention programs, optimize program outcomes, and evaluate program impact.

Microbicides

Microbicides are a class of health products that can create an effective chemical barrier to sexually transmitted infections (STIs) and can be used to address the urgent yet unmet need for protecting women against HIV/AIDS. USAID is a global leader in microbicide R&D and remains committed to supporting the development of safe, effective, acceptable, and affordable microbicide products that are suitable for use in developing-country public sector programs. As such, USAID's activities include:

- Conducting research on preclinical microbicide product development and evaluation
- Developing and assessing safe and acceptable microbicide formulations and modes of delivery

Spotlight: Advancing HIV Prevention Strategies for Women

In many countries, women lack the power to negotiate the use of prevention tools and approaches to protect themselves against HIV – in sub-Saharan Africa, women alone account for 60 percent of HIV infections. Therefore, a need exists for prevention methods that enable women to have greater control over HIV prevention. For more than one decade, USAID has been a global leader in the development of microbicides – products that can be applied vaginally to prevent sexual transmission of HIV – as one of several methods to address this urgent yet unmet need for women around the world.

In 2010, the U.S. Agency for International Development (USAID)-supported Center for the AIDS Program of Research in South Africa (CAPRISA) 004 trial in South Africa provided the first-ever proof that a microbicide, Tenofovir 1-percent vaginal gel can safely and effectively protect women from HIV transmission. The trial compared the use of Tenofovir 1-percent vaginal gel versus a placebo gel in 889 women at high risk of HIV infection, and Tenofovir 1-percent vaginal gel was shown to be 39 percent effective in reducing a woman's risk of acquiring HIV; effectiveness increased to 54 percent among women who used the product very consistently. Tenofovir 1-percent vaginal gel also was found to be 51 percent effective in preventing genital herpes infections in these women. If these significant protective effects are confirmed in further studies, widespread use of Tenofovir 1-percent vaginal gel at this level of protection could prevent more than one-half million new HIV infections in South Africa alone over the next decade.

USAID will continue to work with the U.S President's Emergency Plan for AIDS Relief, multilateral agencies, and partner countries to ensure this breakthrough in HIV prevention, and the full impact of its effects, can be offered to vulnerable women and girls worldwide, especially in low-resource settings.

Table 1. USAID Cooperative Agreements for Microbicide Research and Development

USAID Cooperating Agency	FY06 Funding ($ thousands)	FY07 Funding ($ thousands)	FY08 Funding ($ thousands)	FY09 Funding ($ thousands)	FY10 Funding ($ thousands)
Population Council	7,150	7,227	6,505	7,317	8,000
CONRAD	14,097	13,982	13,506	15,560	12,000
Family Health International	13,776	12,551	14,914	16,683	17,510
WHO	100	406	837	700	600
Global Campaign for Microbicides	735	728	905	919	800
Int'l Partnership for Microbicides	2,347	2,500	3,269	1,000	3,750
CDC	623	1,405	2,715	1,120	500
PATH	286	676	1,004	1,075	458
AIM Project	186	125	351	253	0
Alliance for Microbicide Development	300	0	580	323	0
GH Tech	0	0	50	50	30
CAMI	0	0	0	0	352
Biomed APS (Partners TBD)	0	0	0	0	1,000
TOTAL	**39,600**	**39,600**	**44,636**	**45,000**	**45,000**

Table 2: Phase IIB/ III Microbicide Studies Currently Supported by USAID

	Tenofovir 1% Vaginal Gel	Oral Truvada in Women
Location of Sites	South Africa	Kenya Tanzania South Africa
Start of Screening and Enrollment	May 2007	July 2008
Number of Participants Enrolled	889	3,900
Final Report Expected	Mid FY 2010	Early FY 2012
USAID Partner Conducting Trial	Family Health International, CONRAD, CAPRISA	Family Health International

- Carrying out clinical studies of potential microbicide products for safety, effectiveness, and acceptability
- Conducting relevant behavioral research

USAID's role in microbicide development is coordinated through extensive representation in and collaboration with the efforts of other U.S. Government agencies, as outlined in the 2006 *Report to Congress: Health-Related Research and Development Activities at USAID*.

Since early 2004, USAID had moved five promising microbicide candidates – Carraguard™, Ushercell™ (cellulose sulfate), Savvy™ (C31G), Tenofovir 1-percent vaginal gel, and oral Truvada – into the final stages of clinical testing in international trials for their safety, effectiveness, and acceptability in reducing the risk of HIV transmission, as indicated in the table "Areas of Research and Introduction: Five-Year Strategy." Trials for Savvy™ and Ushercell™ were ended, respectively, because completion at the sites chosen became futile and because safety concerns became apparent only in the larger trial. Carraguard™ was found to be safe and acceptable, but it did not significantly prevent HIV infection.

In 2010, USAID made a historic breakthrough: Results from the CAPRISA 004 trial provided the first-ever proof that a microbicide, Tenofovir 1-percent vaginal gel,

could safely and effectively reduce women's risk of HIV infection, as further described above in "Spotlight: Advancing HIV Prevention Strategies for Women." Once these results are confirmed in further studies, this microbicide could be a unique HIV prevention tool for women who are not able to negotiate other HIV prevention methods with their male partners. USAID continues to work with all partners to ensure that this new technology becomes available to vulnerable women and girls as soon as possible.

USAID also is continuing to evaluate the safety and effectiveness of pre-exposure prophylaxis (PrEP) for women, using oral Truvada – a combination of Tenofovir and emtricitabine – in what is known as the FemPrEP trial. This microbicide product is also antiretroviral (ARV)-based and is delivered orally, which potentially may increase both user compliance and product effectiveness. The FemPrEP trial is expected to enroll 3,900 women at sites in Kenya, Tanzania, and South Africa, and will be completed in 2012, as further discussed in Table 2.

Other next-generation ARV-based microbicide leads are in the product development pipeline and will be tested clinically if they continue to show good results in preclinical testing. USAID's support for the International Partnership for Microbicides is particularly instrumental in advancing these early and promising leads.

In accordance with USAID's strategic plan, during the next year, a large part of the Agency's microbicide development R&D budget will continue to support clinical studies of promising products. The remaining funds will be used to advance research on selected next-generation microbicide leads; novel delivery methods (such as vaginal rings, tablets, and films); combination products that include both multiple mechanisms of action and multiple-purpose agents (to prevent pregnancy and STIs as well as HIV); understanding and prevention of the risk of viral resistance; novel non-ARV leads; and optimized clinical trial design and trial site coordination. Some funds also will be used to prepare for the policy and regulatory requirements that will need to be addressed for the approval and introduction of these new products when they are shown to be safe and effective.